

Neuroprotective effect of placenta-derived mesenchymal stromal cells: role of exosomes.

Journal: FASEB J

Publication Year: 2019

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PubMed link: 30753093

Funding Grants: Placental Stem Cells for the In Utero Treatment of Spina Bifida, Placental Mesenchymal Stem Cell Augmentation of Fetal Myelomeningocele Repair

Public Summary:

We have established early gestation placental stem cells as a potential treatment for spina bifida (SB), a spinal column defect that leaves children with lifelong lower limb paralysis, cognitive deficits, and bowel and bladder incontinence. Our preclinical studies demonstrated that PMSCs have the potential to cure hind-limb paralysis in a sheep SB model before birth. PMSCs act by secreting neurotrophic factors. PMSCs exhibit neuroprotective function by increasing cell number and neurites in vitro. In addition to neurotrophic factors, PMSCs also secrete extracellular vesicles called exosomes, which contain several proteins and RNAs involved in neuronal development and survival. Like PMSCs, exosomes also increase neurite outgrowth, suggesting that they exhibit neuroprotective function. Galectin 1, a neuroprotective and immunomodulatory protein, is present on the surface of PMSCs and exosomes. This protein binds to neuronal cells and imparts the neuroprotective function.

Scientific Abstract:

We have established early-gestation chorionic villus-derived placenta mesenchymal stromal cells (PMSCs) as a potential treatment for spina bifida (SB), a neural tube defect. Our preclinical studies demonstrated that PMSCs have the potential to cure hind limb paralysis in the fetal lamb model of SB via a paracrine mechanism. PMSCs exhibit neuroprotective function by increasing cell number and neurites, as shown by indirect coculture and direct addition of PMSC-conditioned media to the staurosporine-induced apoptotic human neuroblastoma cell line, SH-SY5Y. PMSC-conditioned media suppressed caspase activity in apoptotic SH-SY5Y cells, suggesting that PMSC secretome contributes to neuronal survival after injury. As a part of PMSC secretome, PMSC exosomes were isolated and extensively characterized; their addition to apoptotic SH-SY5Y cells mediated an increase in neurites, suggesting that they exhibit neuroprotective function. Proteomic and RNA sequencing analysis revealed that PMSC exosomes contain several proteins and RNAs involved in neuronal survival and development. Galectin 1 was highly expressed on the surface of PMSCs and PMSC exosomes. Preincubation of exosomes with anti-galectin 1 antibody decreased their neuroprotective effect, suggesting that PMSC exosomes likely impart their effect via binding of galectin 1 to cells. Future studies will include in-depth analyses of the role of PMSC exosomes on neuroprotection and their clinical applications.-Kumar, P., Becker, J. C., Gao, K., Carney, R. P., Lankford, L., Keller, B. A., Herout, K., Lam, K. S., Farmer, D. L., Wang, A. Neuroprotective effect of placenta-derived mesenchymal stromal cells: role of exosomes.

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